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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/582,047	04/21/2007	Ross G. Clark	TRCA-004	9278

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EXAMINER
GODDARD, LAURA B

ART UNIT	PAPER NUMBER
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/582,047	CLARK, ROSS G.	
	Examiner	Art Unit	
	LAURA B. GODDARD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 16-25* is/are pending in the application.

4a) Of the above claim(s) *6,7,10 and 20-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,8,9 and 16-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 June 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/31/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The response filed on September 15, 2009 to the restriction requirement of July 21, 2009 has been received. Applicant has elected Group I, claims 1-10 and 16-24, and the species of breast cancer, breast tissue, and surgery for examination. Because Applicant did not distinctly and specifically point out any errors in the restriction requirement, the election has been treated as an election without traverse (MPEP 818.03(a)).

Claims 1-10 and 16-25 are pending. Claim 25 has been withdrawn from further consideration by the examiner under 35 CFR 1.142(b) as being drawn to non-elected inventions. Claims 6, 7, 10, and 20-24 are withdrawn as being drawn to non-elected species. Claims 1-5, 8, 9, and 16-19 are currently under prosecution as drawn to the elected species of breast cancer, breast tissue, and surgery.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 3-5, 8, 9, 16-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claims are drawn to a method of **preventing** a prolactin receptor-related condition in a subject in need of such prevention, comprising: administering to said subject a human growth hormone-based prolactin receptor antagonist and zinc in an amount effective to treat such condition.

The specification discloses that a “prolactin receptor-related condition” refers to a condition affected by either systemically or locally increased prolactin concentrations or activity, or locally increased prolactin receptor number or activity, and examples include

cancers such as breast tumors (p. 7-8, [0030]). The specification discloses that "prevention" refers to a reduction in a patient's risk of acquiring a prolactin-related condition, wherein the patient has either a genetic predisposition to a prolactin receptor-related condition or a non-genetic predisposition to the prolactin receptor-related condition. Prevention of breast cancer or prostate cancer also includes actively intervening as described herein prior to onset to prevent such onset of the disease (p. 10, [0042]). The specification discloses a long list of possible human growth hormone-based prolactin receptor antagonists, including mutant G120R (p. 17-20, [0071-0079]). The specification discloses a prophetic example for treating breast cancer comprising administering a "growth hormone-based prolactin receptor antagonist plus active zinc supplementation" (Example, section 7, p. 46-48). The specification provides no working examples for the prevention of any prolactin receptor-related conditions in a subject including breast cancer.

In relevant art, Fuh et al (J of Biological Chemistry, 1995, 270:13133-13137) demonstrate antagonistic activity of human growth hormone mutant G120R on the growth of human breast cancer cells *in vitro* and show that adding zinc to the cells increases the affinity of G120R to prolactin receptor and increases the inhibitory effect of G120r on breast cancer cell growth (p. 13135, col. 2; Figure 3; p. 13136, col. 1, first paragraph; p. 13137, col. 1). Although antagonistic activity of G120R and zinc are demonstrated on the growth of breast cancer cells *in vitro*, the growth of the cells was not prevented.

One cannot extrapolate the disclosure of the specification to the enablement of the claims because the specification provides no guidance or examples for the claimed method to predictably **prevent** any prolactin receptor-related conditions in a subject including breast cancer. Further, the art (Fuh et al above) demonstrate that the administration of G120R and zinc was not able to prevent cell growth, but rather, slowed cell proliferation. A high quantity of experimentation would be required to determine what human growth hormone-based prolactin receptor antagonist in combination with zinc would function to predictably prevent a prolactin receptor-related condition in a subject including breast cancer and no relevant art teaches the enablement of such prevention.

Therefore, in view of the state of the art, the quantity of experimentation necessary, the lack of guidance in the specification, and the absence of working examples, it would require undue experimentation for one skilled in the art to practice the invention as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 1-5, 8, 9, 16, and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 6,429,186, Fuh et al, issued August 6, 2002, in view of Fuh et al (J of Biological Chemistry, 1995, 270:13133-13137).

It is noted that the specification defines breast cancer as a prolactin receptor-related condition (p. 8, line 2, [[0030]).

It is noted that the preamble recitation of a method for "preventing a prolactin receptor-related condition" is merely suggestive of an intended use of the method and is not given weight for purposes of comparing the claims with the prior art. The claims read on the active steps *per se*, which are administering to a subject a human growth hormone-based prolactin receptor antagonist and zinc (see MPEP 2111.02).

US Patent 6,429,186 ('186) teaches a method of treating breast cancer in a patient comprising administering human growth hormone mutant G120R that binds to and antagonizes prolactin receptor (col. 5, lines 13-22; Figures 16-18; col. 24, lines 8-14; Example 12; claims 1, 2, and 6). '186 exemplifies decreasing breast cancer cell growth comprising administering G120R (Example 12; Figures 16-18). '186 demonstrates that the addition of zinc, $ZnSO_4$, increased the antagonistic effect of G120R on breast cancer cell growth (Figure 17b), teaches zinc is required for binding of human growth hormone to the prolactin receptor (col. 42, lines 34-35), and teaches that zinc increases the affinity of human growth hormone to the prolactin receptor (Example 12). '186 teaches methods of sustained release drug administration (col. 23, line 21 to col. 24, line 6). '186 teaches the human growth hormone mutant can be formulated and dosed in a fashion consistent with good medical practices, taking into account the

clinical condition of the patient, the site of delivery of the drug, and the method of administration (col. 24, lines 30-40).

'186 does not teach administering zinc to the breast cancer patient in addition to the G120R human growth hormone mutant or that both are formulated in a sustained release formulation.

Fuh et al demonstrate human growth hormone mutant G120R inhibited the growth of breast cancer cells (Figure 3; p. 13135, col. 2) and the addition of zinc, $ZnSO_4$, increased the antagonistic effect of G120R on breast cancer cell growth (p. 13136, col. 1, first paragraph; Figure 3D). Fuh et al suggest administering G120R to breast cancer patients for treatment, and suggest increasing the affinity of G120R for the prolactin receptor to make it a more potent antagonist, otherwise very high levels of antagonist would be required for clinical use for any substantial growth inhibition (p. 13137, col. 2).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to and one would have been motivated to administer zinc in combination with human growth hormone mutant G120R to breast tissue for the treatment of breast cancer in a subject because G120R inhibits the growth of breast cancer cells and zinc is required for binding of G120R to prolactin receptors in breast cancer. One of ordinary skill in the art would have a reasonable expectation of success treating breast cancer in a subject comprising administering zinc and G120R given '186 and Fuh et al demonstrate the addition of zinc increased the antagonistic effect of G120R on breast cancer cell growth.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to and one would have been motivated to include the zinc with the G120R sustained release formulation taught by '186 in order to make the administration of two agents more efficiently as one administration. One would have a reasonable expectation of success combining zinc with the G120R sustained release formulation given '186 teaches such methods of drug formulation and administration are known in the art and provides numerous examples.

4. Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 6,429,186, Fuh et al, issued August 6, 2002, and Fuh et al (J of Biological Chemistry, 1995, 270:13133-13137) as applied to claims 1-5, 8, 9, 16, and 18 above, and further in view of Aamodt et al (The American J of Clinical Nutrition, 1979, 32:559-569).

The claim is drawn to the method of claim 16 wherein said zinc is administered orally.

Fuh et al and '186 (the combined references) teach a method of treating breast cancer (a prolactin receptor-related condition) in a subject comprising administering zinc and G120R in a sustained release formulation as set forth above.

The combined references do not teach administering the zinc orally.

Aamodt et al teach the administration of zinc orally is known and teach that there is no difference in metabolism of zinc whether administered intravenously or orally (abstract).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to and one would have been motivated to administer zinc orally in the method of the combined references because Aamodt et al teach that zinc administration orally is known. One would have a reasonable expectation of success administering zinc orally in the method of the combined references because Aamodt et al demonstrate successful delivery of zinc orally to patients, and zinc metabolism was unaffected by route of administration.

5. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 6,429,186, Fuh et al, issued August 6, 2002, and Fuh et al (J of Biological Chemistry, 1995, 270:13133-13137) as applied to claims 1-5, 8, 9, 16, and 18 above, and further in view of Chen et al (Clinical Cancer research, 1999, 5:3583-3593).

The claim is drawn to the method of claim 4 wherein said antagonist and zinc are administered in combination with surgery.

Fuh et al and '186 (the combined references) teach a method of treating breast cancer (a prolactin receptor-related condition) in a subject comprising administering zinc and antagonist G120R as set forth above.

The combined references do not teach combining surgery with the method of treating breast cancer.

Chen et al teach that for decades, the primary therapy for women with breast cancer has been surgery (p. 3583, col. 1, first paragraph).

These references suggest the importance of each of these methods in breast cancer treatment. However, the references are deficient in that they do not teach using these methods together. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use the zinc and G120R antagonist taught by the combined references and the surgery agent taught by Chen et al in combination in order to treat breast cancer. One of ordinary skill in the art would have been motivated to use the zinc/G120R and surgery in combination in a method of treating breast cancer in view of the importance of eliminating tumor cells. Each of these methods had been taught by the prior art to be effective in the treating breast cancer or inhibiting breast cancer proliferation, thus the instant situation is amenable to the type of analysis set forth in In re Kerkhoven, 205 USPQ 1069 (CCPA 1980) wherein the court held that it is *prima facie* obvious to combine two modes of treatment, each of which is taught by the prior art to be useful for the same purpose in order to make a protocol that is to be used for the very same purpose since the idea of combining them flows logically from their having been individually taught in the prior art. Applying the same logic to the instant process claims and composition claim, given the teaching of the prior art of processes using either zinc/G120R or surgery in the process of treating breast cancer, it would have been obvious to treat breast cancer with both zinc/G120R and surgery because the idea of doing so would have logically followed from their having been individually taught in the prior art to be useful as methods for the same

purpose of treating breast cancer. One of ordinary skill in the art would have reasonably expected to obtain effective treatment of breast cancer with either or both of these methods since both are taught in the prior art to be used for treating breast cancer.

6. **Conclusion:** No claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAURA B. GODDARD whose telephone number is (571)272-8788. The examiner can normally be reached on 7:00am-3:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Laura B Goddard/
Primary Examiner, Art Unit 1642